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Case report

Myeloid sarcoma of the tongue as a first manifestation of acute promyelocytic leukemia: A case report

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ABSTRACT

Introduction: We describe a 35-year-old male patient showing a myeloid sarcoma (MS) of the tongue as the first manifestation of acute promyelocytic leukemia (APL). The MS can appear in all parts of the human body, but it is extremely rare in the tongue.
Clinical case: The main symptoms were a pain in the tongue, asthenia, gingivorrhagia, fever. We found a tumor in the tongue, which was irregular in size and located in the posterior region of the right lateral edge of the tongue. The diagnosis of MS was made by the anatomopathological and immunohistochemical study, while the definite diagnosis of APL was confirmed by the molecular test. The treatment of APL was based on the administration of trans-retinoic acid 45 mg/m^2 daily continuously and daunorubicin 60 mg/m^2 every other day for 4 doses, with a favorable therapeutic response to APL and MS.
Conclusion: Promyelocytic myeloid cells can infiltrate many organs extramedullary, such as the tongue, and this might precede bone marrow infiltration. The early identification of myeloid sarcoma allows to carry out an early treatment of the APL.

1. Introduction

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia in which abnormal promyelocytes predominate. APL distinguishes for a good prognosis and high cure rates.[1,2] Myeloid Sarcoma (MS) is a localized tumor, characterized by extramedullary infiltration of immature myeloid cells.[3,4] In Latin America, a higher frequency of APL is described with regard to the rest of the world, ranging from 20 % to 25 % of all cases of acute myeloid leukemia.[5] In the United States, frequencies between 5 % and 13 % are reported.[6] In Peru, a study has reported a frequency of 22 %.[7] MS has been reported in 2,5 and 8,0 % of patients with acute myeloid leukemia (AML)[4] The most common MS infiltration sites include the central nervous system, the skin, lymph nodes, soft tissues, bones and periosteum, orbit, ovaries, myocardium, and others.[8–15] However, APL is extremely rare in the tongue.[16] We describe a 35-year-old male patient that shows a MS involving the tongue as the first manifestation of APL.

2. Clinical symptoms and physical examination

We present a 35-year-old male patient, a construction worker, born in the forest region of Loreto, from Lima, Peru. He has a medical background of Helicobacter pylori gastritis, which he suffered in 2015. The patient went to the Alberto Sabogal Sologuren National Hospital (ASSNH), reporting a lesion in the tongue that caused pain and had increased progressively in size for 36 days. He had fever and gingivorrhagia a day before emergency admission, and the pain in the tongue increased. On physical examination, there was evidence of fever, paleness of skin and mucosa, gingivorrhagia, petechiae, and ecchymosis in the upper and lower limbs. We found neither lymphadenopathies nor visceromegaly or deep venous thrombosis. In the oral cavity, an irregular exophytic tumor of 3 cm × 4 cm was

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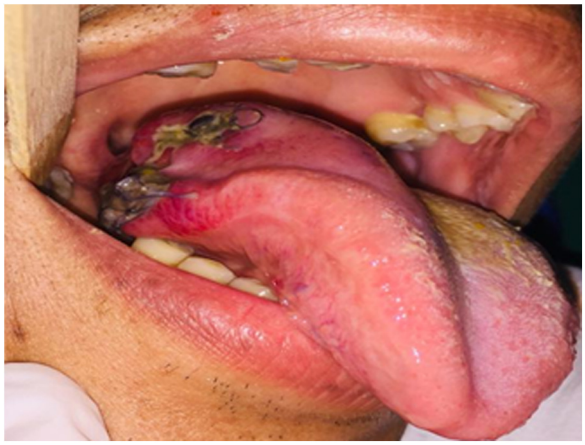

Fig. 1. Myeloid sarcoma of the tongue before treatment.

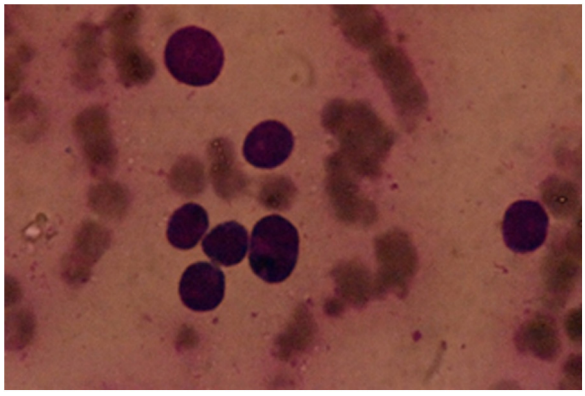

Fig. 2. Bone marrow aspiration: hypercellular bone marrow infiltrated by abnormal promyelocytes, hypergranular in more than 90 %, some Auer canes, which displace the three cell lines.

found on the dorsal lingual side and the edge of the tongue with a necrotic surface and non-defined edges, and a red-bluish ulcer of soft tissue consistency, which was painful on palpation (Fig. 1).

3. Diagnosis of acute promyelocytic leukemia

The blood tests on admission to ASSNH showed the following results: hemoglobin: 5.3 g/dl, platelet count: 10,000 × mm^3, leukocytes: 10,200 × mm^3 (blasts: 52 %, promyelocytes: 43 %). We carried out a bone marrow aspiration in which the presence of hypercellular bone marrow infiltrated by promyelocytes was found in more than 90 %. (Fig. 2).

Flow Cytometry revealed an immature myeloid population of aberrant phenotype, representing 97.36 % of the whole nuclear

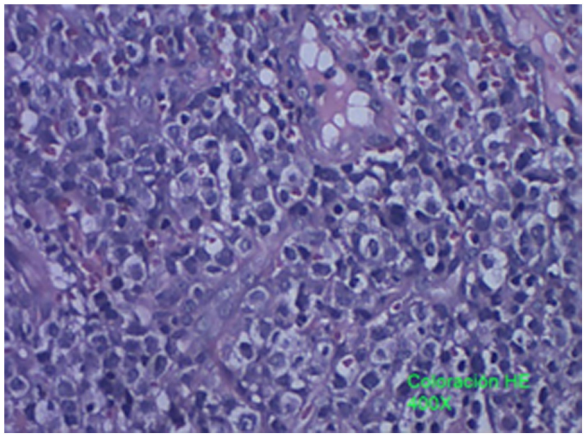

Fig. 3. Atypical ovoid-shaped cell proliferation is compatible with myeloid sarcoma.

cells. Phenotyping was correlated with aberrant promyelocytes showing hypergranular (40 %) and hypogranular (60 %) variants.

We confirmed the diagnosis by evidence of translocation t (15; 17) (q22; q21) in cytogenetic analysis, and PML/RARA gene mutation detected by polymerase chain reaction (PCR) test (molecular analysis).

4. Diagnosis of myeloid sarcoma

We could observe atypical ovoid-shaped cell proliferation in the histopathology of the tongue (Fig. 3). Likewise, immunohistochemistry for myeloid markers showed CD68 + Ki67 + (88 %), CD15+, and myeloperoxidase (MPO) + (Fig. 4).

Additionally, the venous Doppler ultrasonography of the lower extremities did not find deep venous thrombosis and the CT-scan in the cervical region did not show masses and/or metastatic infiltration.

5. Therapeutic intervention and follow-up

Therapeutic intervention with previous informed consent by the patient consisted of daunorubicin 60 mg/m2 every other day for 4 doses and trans-retinoic acid (ATRA) 45 mg/ m2 and during 90 days or until reaching complete morphological and molecular remission.[17]

The patient was discharged 48 days after being hospitalized. The results of blood tests at discharge were: hemoglobin: 9.5 g/dl, platelet count: 649,000 xmm3, leukocytes: 2,330 xmm3, (blasts: 0 %, promyelocytes: 0 %), HDL: 344U/L, creatinine: 0.62 mg%, C-reactive protein: 0.25 mg/dl. The evolution of the MS was favorable (Fig. 5).

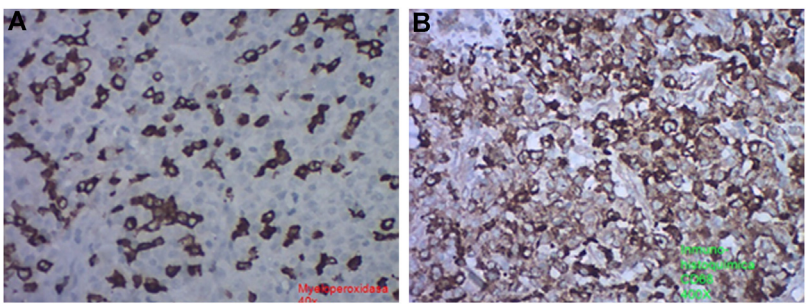

Fig. 4. A. Histopathology of the tongue showing myeloid marker MPO +, B. Histopathology of tumor cells showing CD68 positive (110 %), as a surrogate myeloid marker.

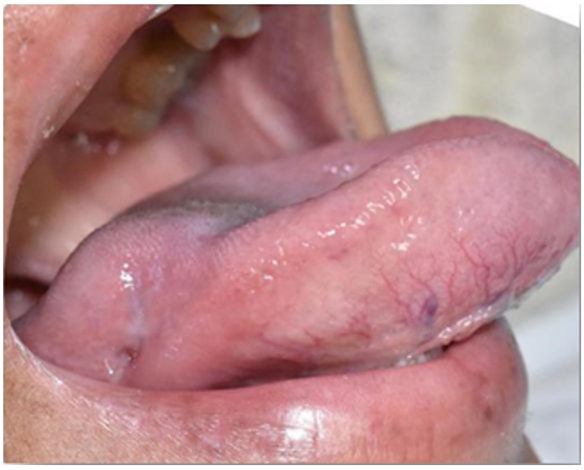

Fig. 5. Myeloid sarcoma at discharge time (48 days after starting treatment).

6. Discussion and conclusions

MS is a rare entity that can appear as an isolated extramedullary tumor composed of immature granulocytic cells. It was first described in 1812 and it was named chloroma later on due to its green color attributed to the presence of myeloperoxidase enzymes.[18] Besides, it can be associated with myelodysplastic syndromes, chronic myeloid leukemia, myeloproliferative dysplasia, and or bone marrow involvement.

The strength of our case report is that leukemic infiltration in the tongue is extremely rare. Only one case report related to APL and MS in the tongue was identified in a 45-year-old male patient with a week's history of dysphagia and painful tongue. The oropharyngeal examination revealed a previous ulcerated tongue. A biopsy was performed and histology demonstrated a cellular infiltration spreading to the muscle fibers; staining was positive for myeloid markers including CD45, myeloperoxidase (MPO), and CD68. The histological diagnosis was MS. The bone marrow was infiltrated by abnormal promyelocytes and acute promyelocytic leukemia was confirmed by flow cytometry (MPO +, CD33 +, CD117 +, CD34) and HLA DR) and cytogenetic analysis: translocation t (15; 17) (q22; q12) and molecular test (PMLRARa gene mutation).[16]

To demonstrate the suspicion of infiltration of promyelocytic cells in the tongue, we had to confirm the presence of myeloid infiltration markers by means of histochemistry: CD68 positive, KI67: 88 % positive, CD15: positive, and myeloperoxidase (MPO) positive.

The common clinical characteristics of APL are pancytopenia, a tendency to abnormal bleedings, and disseminated intravascular coagulation (DIC); these last parameters are considered to be responsible for most of the early deaths in this pathology and are the main challenge to overcome when APL is suspected.[12] Our patient was admitted with a mild gingivorrhagia, but he did not present DIC.

Literature reports the presence of MS associated with gingival hyperplasia and lesions of the oral cavity.[11,12] These clinical manifestations led the patient to look for an early dental consultation. Although the doctors diagnose leukemia more frequently, the role of dentists is important to get to the diagnosis of MS since it can precede the systemic manifestations of APL.

The distinguishing characteristic of APL is the presence of alteration of chromosome t (15; 17), which results from the fusion of the promyelocytic leukemia gene and the trans-retinoic acid receptor alpha (RAR alfa) gene, being the molecular objective of the treatment with trans-retinoic acid (ATRA). In our patient, the molecular diagnosis was confirmed by cytogenetics and molecular test.[19,20]

According to scientific literature, APL is the subtype with best prognosis of all acute myeloid leukemias. The APL with PML/RARA is classified as a favorable risk group of acute myeloid leukemia (AML) with a greater rate of total remission of more than 90 % and a general survival rate of more than 80 % in a 5-year period. Our patient had a favorable response to therapeutic intervention with trans-retinoic acid (ATRA), regarding the clinical setting of APL and MS.[21,22]

The relevance of our case report is based on the fact that oral lesions might represent the first manifestations of acute myeloid leukemia. Thus, the early identification of infiltrative lesions in the oral cavity might improve the diagnosis of APL and promote an early treatment knowing this condition has a better prognosis than other types of leukemia. Dentists have a critical role in the diagnosis considering the progression of the disease. This case puts emphasis on the need for oral health care professionals to be familiarized with the clinical manifestations of acute leukemia and guarantee its early detection and referral to health care services.

Finally, as evidenced in our case report, the treatment of acute promyelocytic leukemia with trans-retinoic acid and chemotherapy improves the disease as well as the myeloid sarcoma.

Conflict of interest

None declared.

Financial disclosure

None declared.

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